PHYSIOLOGICAL ACTION OF LYCOCTONIA.

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LYCOCTONIA and napellina were distinguished as separate alkaloids from aconitia by Hüschmann. He procured them from Aconitum lycoctonum. The specimen used by me was made by Trommsdorf, and was a white crystalline powder. Bromine-water added to it gave a yellow precipitate, Nessler's reagent precipitated it largely, sulphuric acid gave a colorless solution, as did also phosphoric with heat. In the succeeding experiments each cubic centimetre of our neutral solution contained a centigramme of the alkaloid in shape of acetate. Klebs made some unpublished experiments with it, and inferred that it was much less energetic than aconitia.

Bucheim and Eisenmenger* made a few experiments on frogs. They saw muscular movements, convulsions, extended extremities, loss of reflex action, with the presence of muscular contractility, contracted pupil, and few respirations. They used doses varying from .0015 to .005 gramme.

Schroff† saw in two men .05 gramme of the acetate produce at first an increased frequency of pulse. In a rabbit .4 gramme by mouth produced increase of pulse and decrease of respiratory movement, with subsequent fall of the former. The pupil was dilated, and the movements wholly undisturbed; the animal recovered.

In another rabbit .4 gramme subcutaneously caused dilated pupil, very frequent pulse and respiration. With doses of .005 to .06 gramme subcutaneously in frogs, sensibility remained intact, the spinal cord appeared not directly affected, the motor nerves were paralyzed, muscles excitable, pupil contracted, disappearance of respiratory movements, heart beating for a very long time after the absence of every sign of life.

Exp. I.—Frog. Weight, sixteen grammes; at 8.46 A.M. received .05 gramme lycoctonia subcutaneously; leaps away; respiratory movements less frequent. 8.49 A.M., complete relaxation; pupil contracted, respiratory movement now and then. 9 A.M., death; motor nerves not irritable; heart beat forty-eight per minute, and was beating still an hour afterwards.

Exp. II.—Frog. Weight, 29.3 grammes; at 8.42 A.M. received subcutaneously .1 gramme of lycoctonia. 8.45 A.M., respirations less frequent; lying on abdomen; great want of co-ordination; loss of movement in posterior extremities. 8.50 A.M., pupil contracted; occasional respiratory movement. 9.5 A.M., .1 gramme under the skin in the vicinity of the lymph-sacs. Mechanical irritation causes muscular twitchings. 9.53 A.M., death; motor nerves irritable only with strongest currents of Dubois's induction-apparatus with Helmholtz's arrangement; thrusting probe down the spine caused no movement; heart beat thirty-two per minute, and continued its movements for over an hour.

The above experiments represent the action of lycoctonia, that it paralyzes the motor nerves or diminishes their irritability.

In the majority of cases I found the motor nerves completely non-irritable; but in some frogs, without regard to species, and even in the same species, the motor nerves were not completely paralyzed. A similar action has been observed by Boehm on frogs with aconitia.

The heart was always beating, lycoctonia not being a cardiac poison in frogs like aconitia, as the following experiment with the latter shows.

* Eckhard's Beiträge, fünfter Band, zweites Heft.
† Beitrag zur Kenntniss des Aconit.

Exp. III.—Frog. Weight, forty-nine grammes; received subcutaneously at 9 A.M. .025 gramme of aconitia of Menck's in shape of acetate; leaps away; lower jaw drooping. 9.08 A.M., complete relaxation; slight movement on mechanical irritation.

9.15 A.M., death; ventricle in complete diastole, no movement in it; auricle beating now and then.

To study the action on the sensory nerves and spinal cord I used the method of Bernard.

Exp. IV.—Frog. Weight, fifty grammes. At 9.10 A.M., received .1 gramme of lycoctonia, the right iliac artery and vein tied previously. 9.12 A.M., diminished respiration; want of co-ordination and power; pupil contracted; mechanical irritation calls out movement only in leg in which supply of poison is shut off; respirations now and then.

9.43 A.M., death; motor nerves upon which the poison acted non-excitable; gastrocnemii of either side equally irritable; heart beat thirty per minute, and pulsated over an hour afterwards.

Exp. V.—Frog. Weight, thirty-nine grammes; right iliac artery and vein ligated; received at 9.53 A.M. .1 gramme lycoctonia subcutaneously. 9.55 A.M., loss of co-ordination; occasional respiratory movements. 10.14 A.M., pupil contracted from position; pinching causes movement only in the limbs in which the access of the poison has been prohibited. 10.18 A.M., .1 gramme lycoctonia subcutaneously. 10.40 A.M., death; sciatic nerve on left side not irritable, but irritation of its central end called out movements in right posterior extremity; right and left gastrocnemius equally irritable; heart beat twenty-four per minute.

These observations show conclusively that the sensory nerves and spinal cord are not affected by this alkaloid.

To study the action on the muscle I used Marey's myograph and Foucault's regulator, after the method laid down by Marey. In no case did I find any prolongation of the curve as produced by veratria, or as Weyland states takes place under aconitia. Boehm and Wartmann were unable to confirm this discovery of Weyland's.

Exp. VI.—Large rabbit received at 12.32 P.M. .1 gramme of lycoctonia into arterial system; the animal immediately became quiet and was unable to stand.

12.35 P.M., .1 gramme injected into arterial system. 12.42 P.M., .1 gramme injected into arterial system. Convulsions, with clonic contractions of muscles of neck and jaws; respirations ceased. 12.43 P.M., death; heart beating.

Exp. VII.—Small rabbit received, per jugular, .1 gramme of lycoctonia; at 9.43 A.M. unable to maintain an erect posture; convulsive movements; pupil dilating; convulsive action of muscles about the neck; respiratory movements ceased.

9.57 A.M., death, heart beating.

It is evident that lycoctonia is a poison which kills mainly by arrest of respiratory apparatus, as cardiac movements continue after death.

Circulation.

The action on the circulation was studied on rabbits. I made sixteen experiments. The animals were narcotized by morphia. In all other respects everything was conducted in the same manner as laid down in my paper on gelsemia. The pressure and pulsations are given for periods of fifteen seconds.

Exp. I.—Rabbit. Curare; tracheotomy; artificial respiration; jugular and carotid prepared.

Time.	Pulse.	Pressure.	
A.M.	67	102	
			Lycoctonia .1 grm.
8.20.15	43	66	
8.20.30	37	54	
8.20.45	31	46	
8.21.30	48	42	
8.21.45	47	44	
8.59.00	50	82	
			Lycoctonia .1 grm.
8.59.15	46	82	
9.00.00	33	60	
9.00.15	32	70	
9.06.15	49	60	

Exp. II.—Rabbit. Curare; artificial respiration; carotid and jugular prepared; tracheotomy.

Time.	Pulse.	Pressure.	
A.M.	75	100	
			Lycoctonia .05 grm.
10.05.15	72	98	
10.05.30	59	84	
10.06.00	64	84	
10.08.00	56	90	
10.09.15	66	24	
10.37.30	66	24	

The preceding experiments show that the action of lycoctonia is a reduction of the pulse and pressure. Immediately after the injection the pulse-waves are considerably greater and steeper. In small doses, like aconitia, its action on the heart causes a delirium cordis, that is, periods where the pulse is suddenly greatly slowed whilst the pressure also rises and falls in a manner not to be predicted. Unlike the action of aconitia, the blood-pressure in

rabbits never suffers a preliminary rise. This series of results can happen either by a central or a peripheral excitation of the pneumogastrics. In nicotin and atropin we have an agent that paralyzes the peripheral end of the vagi. Schmiedeberg* has shown that in a heart stopped by muscarin, which greatly excites the cardio-inhibitory ganglia, nicotin is unable to start the heart, whilst atropin does. This led him to infer that nicotin paralyzes the nerves uniting the peripheral end of the vagi to the cardio-inhibitory ganglia, and that atropin paralyzes the ganglia themselves.

Exp. III.—Rabbit. Tracheotomy; curare; artificial respiration; carotid and jugular prepared; vagi cut.

Time.	Pulse.	Pressure.	
A.M.	78	106	
			Lycoctonia .1 grm.
10.45.00	71	90	
10.45.30	48	36	
10.45.45	49	30	
10.46.30	63	30	
10.51.30	75	70	
10.55.45	60	82	
11.17.30	65	72	

Exp. IV.—Rabbit. Tracheotomy; curare; artificial respiration; atropin; carotid and jugular prepared; paralysis of vagi as tested by strong currents.

Time.	Pulse.	Pressure.	
P.M.	60	130	
			Lycoctonia .1 grm.
6.00.15	57	100	
6.00.30	56	68	
6.01.00	50	38	
6.01.15	48	40	
6.10.30	59	120	Coagulation.
6.11.15	60	118	
6.12.00	61	120	
6.12.45	64	118	

Exp. V.—Rabbit. Tracheotomy; curare; vagi paralyzed by nicotin as proved by irritating with strong currents. Carotid and jugular prepared; artificial respiration.

Time.	Pulse.	Pressure.	
A.M.			
9.00.00	70	118	
			Lycoctonia .1 grm.
9.01.00	62	54	
9.01.15	62	55	
9.01.30	67	54	
9.21.53	57	108	Coagulation.

These observations show conclusively that the sinking of pulse and pressure has not its seat either in a central or peripheral stimulation of the cardio-inhibitory apparatus. The peculiar paroxysmal action of the heart continues after the use of atropin. That the vagi are not paralyzed by small doses the following observations show.

Exp. VI.—Rabbit. Tracheotomy; curare; artificial respiration; carotid and jugular prepared; left vagus prepared.

Time.	Pulse.	Pressure.	
P.M.	68	126	
			Lycoctonia .05 grm.
3.50.00	63	126	
3.50.15	78	120	
3.51.00	63	124	
4.06.15	62	96	
4.07.00	62	78	
			Lycoctonia .05 grm.
4.07.15	58	77	
4.07.30	55	64	
4.08.00	57	68	
4.09.30	46	102	
4.12.45	55	108	
			Lycoctonia .05 grm.
4.13.15	61	116	
4.13.30	49	111	Vagus irritated for three seconds. Dubois's secondary coil at 4.
4.19.55	58	120	
			Lycoctonia .05 grm.
4.20.10	63	113	
4.20.25	61	114	
4.21.00	51	110	Vagus irritated for one second. Dubois's coil at 4.
4.24.30	52	130	
			Lycoctonia .05 grm.
4.24.45	58	120	
4.45.19	60	128	
4.45.34	36	110	Vagus irritated four seconds. Dubois's coil at 4.

Exp. VII.—Rabbit. Right vagus prepared; canula in jugular; Middeldorpf's needle used to observe the action of the heart.

Time.	
P.M.	
2.15	Dubois's coil at 11. Stops heart. Lycoctonia .1 gramme.
2.18	Dubois's coil at 11. Slows the heart.
2.24	Lycoctonia .4 gramme.
2.26	Artificial respiration.
2.33	Dubois's coil at 0. slows the heart.
2.43	Dubois's coil at 0. no power over the heart.

Exp. VII. shows that large doses are able to paralyze the vagi, for when the secondary coil was shoved over the primary the pneumogastric had no action on the heart.

Exp. VIII.—Rabbit. Tracheotomy; curare; artificial respiration; carotid, jugular, and sciatic nerve prepared; Ludwig's screw-electrode fastened into the atlas and occiput; Pohl's commutator so arranged that the cur-

* Ludwig's Arbeiten, 1870.

rent of electricity can be sent either to the sciatic nerve or the vaso-motor centre by rolling the cradle.

Time.	Pulse.	Pressure.	
A.M.	57	94	
			Lycoctonia .05 grm.
10.46.15	55	76	
10.46.30	53	80	
10.46.45	51	54	
10.47.30	51	60	
10.52.00 to 11.02.05			Lycoctonia .15 grm.
11.03.10	56	90	
11.03.25	54	102	Vaso-motor centre irritated indirectly for two seconds. Dubois's coil at 16.
11.08.28	44	84	
11.16.01	50	62	Depressor nerve irritated for eleven seconds. Dubois's coil at 16.
11.34.01 to 12.16.56			Lycoctonia .250grm.
12.19.17	40	48	
12.19.32	45	70	Vaso-motor centre irritated indirectly for nine seconds. Dubois's coil at 16.
12.24.36	54	94	
12.24.51	45	120	Vaso-motor centre directly irritated for six seconds. Dubois's coil at 5.

In Exp. VIII. I have tried to see if the alkaloid paralyzes the vaso-motor centre. Unlike aconitia, it does not, either to direct or indirect irritation. It is quite probable that enormous doses might do so; but that large doses do so is not tenable. This experiment also confirms the view that this poison does not act on the sensory nerves or the spinal cord.

Exp. IX.—Rabbit. Tracheotomy; curare; artificial respiration; carotid and jugular prepared; all cardiac nerves in neck are cut; cord cut between the atlas and occiput; hemorrhage checked by bovista.

Time.	Pulse.	Pressure.	
P.M.	54	52	
			Lycoctonia .1 grm.
2.08.15	42	52	
2.08.30	37	34	
2.08.45	26	28	
2.09.30	33	19	
2.15.15	30	22	

In the ninth experiment the heart is entirely freed from its afferent and efferent nerves. Here the same change takes place, —that is, fall of pulse and of pressure.

It is evident that the fall of pressure and of pulse is due to diminished excitability of the heart, and, as the striated muscles are not affected by the poison, it must be due to the nervous mechanism being changed. But how are we to explain the paroxysmal changes of pulse and pressure, the delirium cordis? Heidenhain, on irritating directly the vaso-motor centre after previous section of the vagi and artificial respiration, observed the following: when strong currents were used there ensued a want of rhythm similar in appearance to that observed after the use of lycoctonia. He had to deal with a high pressure in the circulatory system. He then sought out the cause of this want of rhythm, whether it was seated in the cardiac nerves or the heart itself. After separation of the cardiac nervous apparatus external to the heart, he found it to be localized in the heart itself. He then thought it must be either in a weakening of the motor ganglia of the heart or increased action of the inhibitory ganglia. The weakening of the motor ganglia seemed to him to fail utterly in accounting for this appearance. His conclusion was that high pressure irritates the cardio-inhibitory ganglia, and thus causes these paroxysms, but when their excitability sinks the want of rhythm disappears; that this delirium is an expression of the antagonism of the forces of the cardio-motor and cardio-inhibitory ganglia, and irritation of the vagi for very short periods gave curves precisely similar. Atropin did not prevent this want of cardiac rhythm, which caused Heidenhain to doubt if it paralyzed all the inhibitory ganglia. Boehm and Wartmann, who observed a similar want of rhythm after small doses of aconitia, think that it is probable that an excitation of the cardio-inhibitory apparatus is called into play, or that aconitia antagonizes the paralytic effect of atropin.

Mr. Lewin explains the want of rhythm after aconitia by an action at dissimilar times and unequal in strength upon one or the other intracardiac nervous apparatus, probably produced by an unequal division of the alkaloid in the blood. It is difficult to see how an unequal distribution of this poison in the circulatory system can occur. It cannot be through any change in the coronary vessels, as the same paroxysms occur in a frog's heart, which has been shown by Hyrtl to be devoid of blood-vessels. Certainly in the case of lycoctonia high

pressure does not irritate the inhibitory mechanism, and atropin does not prevent the want of rhythm. Either one must assume that atropin does not completely paralyze all the inhibitory ganglia, or that lycoctonia antagonizes it.

To my mind neither explanation is sufficient. The recent experiments of Bowditch, Luciani and Rossbach and Kronecker, seem to be near the discovery of the real cause.

The following expresses my conclusions in regard to this poison:

1. Lycoctonia is a weaker toxicant than aconitia.

2. That it kills mainly through the respiratory apparatus.

3. That it paralyzes the motor nerves.

4. That it does not affect the sensory nerves, spinal cord, or the striated muscles.

5. That it reduces the blood-pressure and pulse without any previous rise of the former as produced by aconitia.

6. That the decreased pulse-rate and pressure are due to an action on the intracardiac nervous apparatus.

7. That the pneumogastrics are paralyzed only by large doses.

8. That the delirium cordis produced by small doses is due to a change in the mechanism of the nervous apparatus of the heart.

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FIG. 1.

FIG. 1.—Pulse-curve of rabbit just before injection; artificial respiration; curare.

FIG. 2.

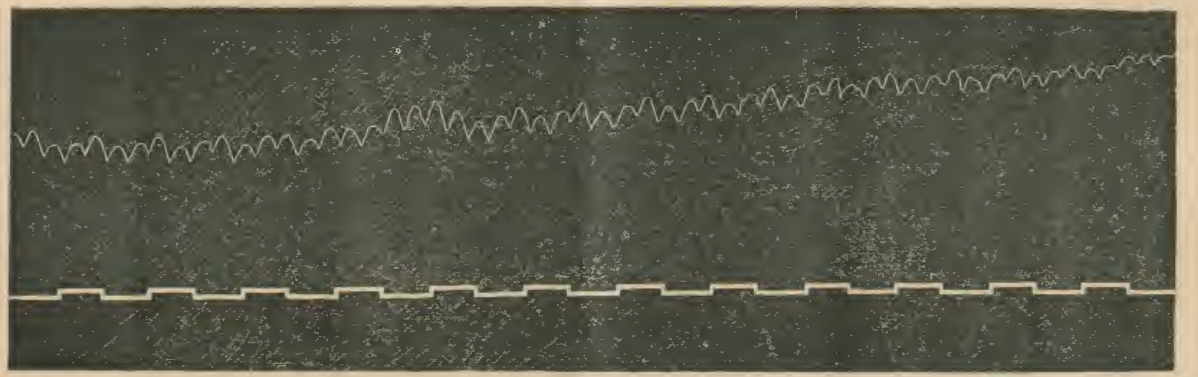


FIG. 2.—Pulse-curve of rabbit seven seconds after injection of .1 gramme of lycoctonia; curare; artificial respiration.

FIG. 3.

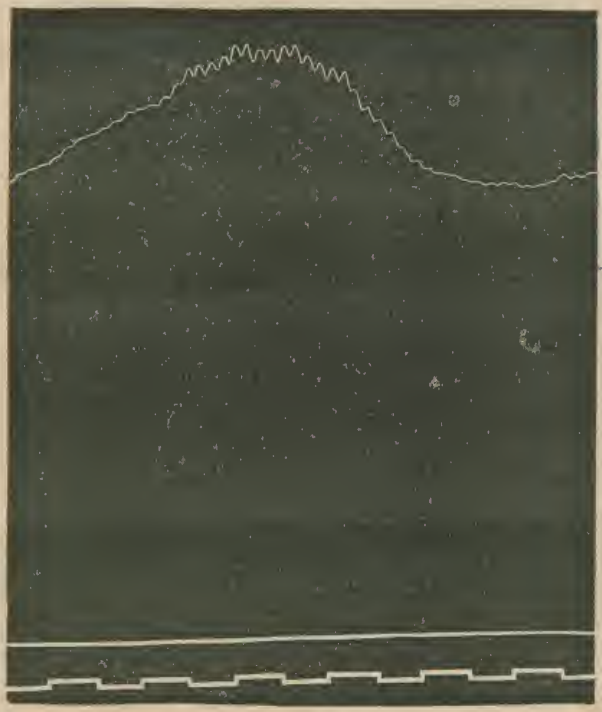
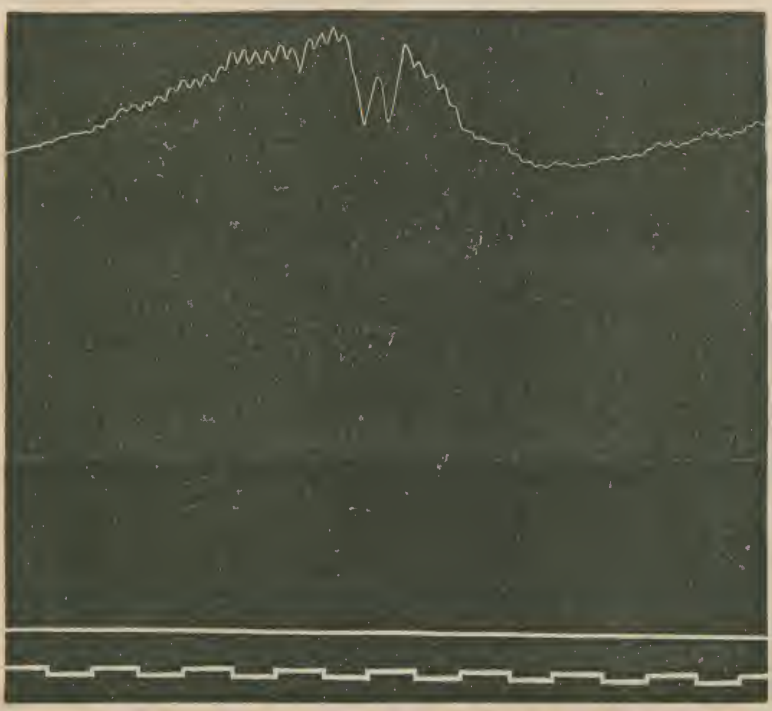


FIG. 4.



FIGS. 3 and 4.—The delirium cordis of rabbit produced by small doses of lycoctonia.